

### **REMARKS**

Reconsideration of this application, as amended, is respectfully requested. Claim 1 has been amended. Claim 34 has been cancelled and the subject matter thereof incorporated into amended claim 1. With this amendment, claims 1, 2, 4-19, 21-27, and 32, 33 and 35 are pending in this application. These amendments are made without prejudice or disclaimer and do not include any new matter. Applicants reserve the right to prosecute any cancelled or otherwise unclaimed subject matter in this or another application. Consideration and entry of this amendment is respectfully requested.

### **REJECTIONS UNDER 35 U.S.C. 103(a)**

#### **A. Claims 1, 2, 4-19, 21-27 and 32-35**

Claims 1-2, 4-19, 21-27, and 32-35 stand rejected under 35 U.S.C. 103(a) over Hurpin, et al. (Vaccine, 16(2/3): 208-215 (1998)) in view of Hodge (Vaccine, 15(6/7): 759-768 (1997)), Rice (U.S. Pat. No. 6,127,116 (1997)), and Lehner, et al. (J. Inf. Dis. 179 (Suppl. 3): S489-S492 (1999)). Claim 34 has been cancelled and the subject matter thereof incorporated into amended claim 1; the rejection is therefore moot as to claim 34. Applicants respectfully traverse the remaining rejections as indicated below.

The Office Action indicates that Hurpin would have provided the skilled artisan with a reasonable expectation that administration of antigen to a lymphatic tissue would be a successful route of administration. As Hurpin does not teach a prime-boost regimen, Hodge is cited as teaching the use of two different poxviral vectors to generate an immune response. As neither of these references teaches direct intranodal administration of antigen, both Rice and Lehner are cited. Rice is cited to teach direct intranodal administration as a preferred immunization route. Lehner is cited to provide a reasonable expectation of success in using intranodal immunization by demonstrating success using their "targeted iliac lymph node" or "TILN" technique. This combination of references is cited as rendering the subject matter of this application obvious. As described below, Applicants respectfully disagree.

Regarding Hurpin, Applicants agree with the statement in the Office Action that the spleen is a type of lymphatic tissue. However, Applicants respectfully disagree that "the skilled artisan, having read Hurpin et al. would have expected that delivery of a

vaccine to a lymphatic tissue, whether splenic or lymph node, would be capable of generating an increased immune response over subcutaneous delivery”. Hurpin’s demonstration of intrasplenic delivery of antigen would not have provided the skilled artisan with any expectation of success in vaccinating a human being in any organ other than the spleen. The skilled artisan would have understood the spleen and lymph node to be very different types of lymphatic tissue and vaccination by direct administration to the spleen not to be predictive of vaccination directly into a lymph node. It also would have been understood by those of skill in the art that intrasplenic administration had little relevance in the human vaccination protocols due to significant safety concerns.

It is understood that Hodge has been cited to show prime-boost, but Hodge does not satisfy the deficiencies of Hurpin, and adds nothing to the similarly insufficient disclosures of Rice and Lehner. Hodge merely demonstrates administration of two different viruses by tail scarification in mice.

Rice does not satisfy the deficiencies of Hurpin. Applicants respectfully disagree that *PharmaStem* holding is not applicable to the instant case. Applicants maintain that Rice’s disclosure is simply “general guidance as to the particular form of the claimed invention”. As previously stated, all that Rice provided the skilled artisan is mere mention of administration “directly...to lymphoid tissues, e.g., lymph nodes...” and nothing more. It is difficult to envision this statement as anything more than “general guidance” as to a potential route of administration, “preferred” or otherwise. In addition, Rice relates only to antigens of infectious organisms while Applicants’ claimed method relates to tumor antigens (e.g., self-antigens). And, as described above, Hurpin’s description of intrasplenic administration of antigen is not predictive of success in directly administering antigen to lymph nodes, and is also of little relevance with respect to vaccination of humans.

Lehner similarly does not satisfy the deficiencies of Hurpin. Lehner states that their process administers antigen “in the proximity of” particular lymph nodes. The skilled artisan would have understood the significant differences between Lehner’s TILN methodology and direct administration into a lymph node. Lehner’s TILN methodology is a subcutaneous administration method that would have been understood to require the assistance of antigen presenting cells (APCs) present in the skin, such as dendritic cells,

to be transported to the lymph node. The skilled artisan would have understood that the TiLN method took advantage of such APCs to present antigen to immune effector cells. In contrast, Applicants' method does not utilize such APCs to transport antigen to the lymph node as it is deposited directly therein. It is also noted that Lehner's method utilized adjuvanted VLPs containing antigen from an infection organism (e.g., not a tumor antigen, or self-antigen). Adjuvant is not required in the claimed method (e.g., instant claim 33). Lehner's method is very different from the claimed method and is not predictive of success resulting from the claimed method. Given these significant differences, Applicants do not believe Lehner is of little relevance to the claimed method and does not satisfy any deficiencies of Hurpin.

Applicants respectfully maintain that the cited references would not have provided the skilled artisan with any expectation that delivery of a vaccine to a lymph node would successfully immunize a human being. Applicants respectfully maintain that a proper *prima facie* showing of obviousness cannot be made by combining Hurpin with Hodge, Lehner and / or Rice. Accordingly, it is respectfully requested that these rejections be withdrawn.

#### **B. Claims 18-19**

Claims 18 and 19 stand rejected under 35 U.S.C. 103(a) over Hurpin in view of Hodge, Rice, and Lehner, as applied in part A above and further in view of Zaremba, et al. (Cancer Res. 57: 4570-4577 (1997)) and Salgaller, et al. (Cancer Res. 56: 4749-4757 (1996)). Applicants respectfully traverse these rejections as indicated below.

Applicants have discussed the deficiencies of the rejection based on the combination of the Hurpin, Hodge, Rice and Lehner references above. As described therein, Applicants do not believe that the alleged combination of references support a proper *prima facie* case of obviousness. And Applicants do not believe Zaremba's disclosure of the peptide YLSGADLNL and / or Salgaller's disclosure of the peptide YLEPGPVTV satisfy the deficiencies of the base combination of references. Accordingly, it is respectfully requested that these rejections be withdrawn.

**C. Claims 21-27**

Claims 21-27 stand rejected under 35 U.S.C. 103(a) over Hurpin in view of Hodge, Rice, and Lehner as applied as applied in part A above and further in view of Barnett (Vaccine, 15(8): 869-873 (1997)). Applicants respectfully traverse these rejections as indicated below.

Applicants have discussed the deficiencies of the rejection based on the combination of the Hurpin, Hodge, Rice and Lehner references above. As described therein, Applicants do not believe that the references can be combined to render the pending claims obvious. And Applicants do not believe Barnett's alleged disclosure of a prime/boost vaccination strategy satisfies the deficiencies of this combination of references. Accordingly, it is respectfully requested that these rejections be withdrawn.

**CONCLUSIONS**

Consideration and entry of this response is respectfully requested. Applicants believe the claims are now in condition for allowance, and respectfully request that a Notice of Allowance be issued as soon as possible. The Examiner is encouraged to contact the undersigned if it is believed doing so would assist in the examination of this application.

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